

# Proficiency testing as tool in estimating national public health infrastructure

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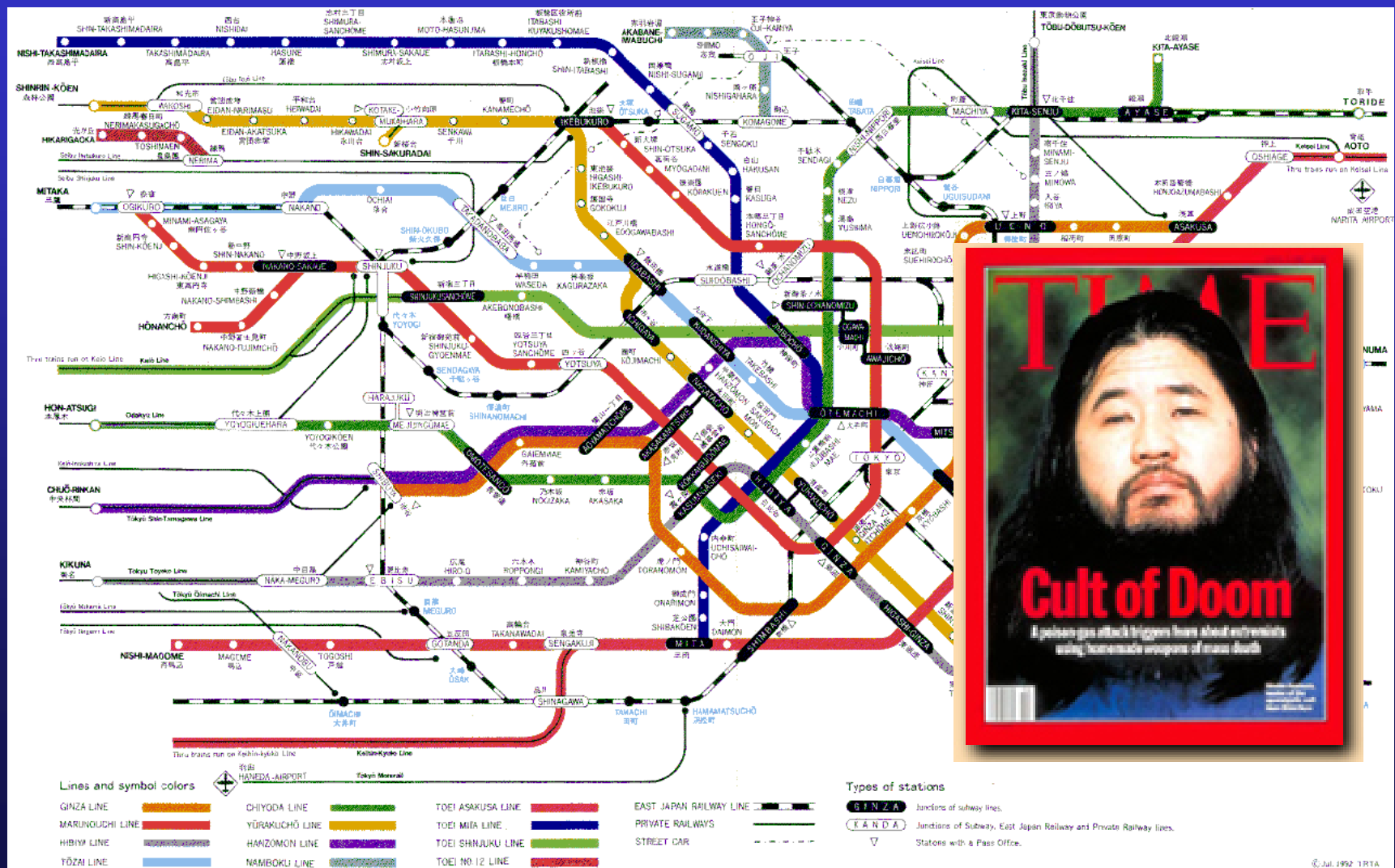
Atlanta, 24 May 2004



**ELEVATED**  
SIGNIFICANT RISK OF  
TERRORIST ATTACKS

# Aum Shinrikyo (オウム真理教)

## Cult Attacks in Japan



# Nerve agents (I)

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- Include Sarin, Soman, Tabun
- Affect transmission of nerve impulses by inhibiting cholinesterase.
- All highly toxic organophosphate compounds that irreversibly bind to cholinesterase, resulting in accumulation of acetylcholine at the nerve synapses and neuromuscular junctions.

# Nerve agents (II)

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- Decreased activity of cholinesterase in blood can be an indicator of exposure to organophosphate inhibitors in cases of chemical terrorism – a sensitive and specific biomarker.
- In the event of such a chemical terrorism act, multiple cholinesterase measurements on serum samples from all potentially exposed subjects will likely be required (also for monitoring recovery).



# ATSDR

## Recommendations



- "Symptomatic and asymptomatic patients suspected of significant exposure should have determinations of red blood cell (RBC) cholinesterase activity, the most useful test for nerve agent poisoning."
- "If this test is not available, plasma cholinesterase can be measured."
- "Patients should be advised to avoid organophosphate insecticide exposure until sequential RBC cholinesterase activity (measured at weekly to monthly intervals) has stabilized in the normal range, a process that may take 3 to 4 months after severe poisoning."

# Kasumigaseki Station Sarin Attack: Numbers

- Over 6,000 injured
- Cholinesterase measurements in injured individuals alone:
  - 6,000 persons
  - Initial test = 6,000
  - Twice monthly/four months = 48,000
- Total = 54,000 measurements



# Estimating Laboratory Infrastructure: Four Approaches

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1. Questionnaires of target population
2. CLIA'88 registry from HHS (CMS [fka HCFA] )
3. Existing databases from CDC, APHL, etc,
4. Proficiency testing surveys



# Estimating Laboratory Infrastructure:

## 1. Surveys of Target Population

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- Require considerable effort to mount
- Response rate often poor
- Appropriate personnel responding?
- Information is stale in two years, requiring yet another survey!

# Estimating Laboratory Infrastructure:

## 2. CLIA Registry from HHS (CMS)

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- Large existing database
- All medical laboratories
- Relatively current
- No information on scope of testing and methods used

# Estimating Laboratory Infrastructure:

## 3. Databases from CDC, APHL, etc,

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- Existing databases would not require new surveys
- Focus on public health laboratories
- Data likely not up-to-the minute
- General rather than specific information

# Estimating Laboratory Infrastructure:

## 4. Proficiency Testing Surveys

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- Required by CLIA'88
- All laboratories must participate in available testing for tests offered
- Conducted three times per year
- Laboratorians respond to the survey
- Information on methodology
- Quality of testing also assessed

# Laboratories in NY Program\*

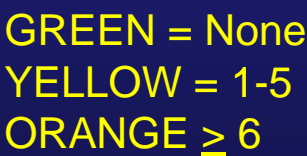
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Within NY State:	800
Outside NY State:	200
Total:	1000

Permit in Clin Chem: 550

\* Rounded numbers

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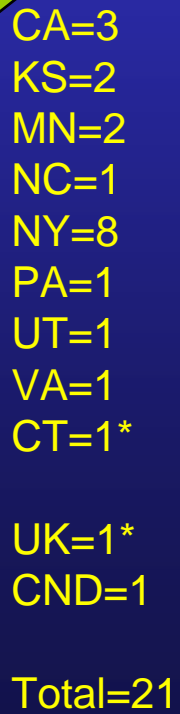


# Cholinesterase Proficiency Testing

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- Cholinesterase is not a regulated analyte under CLIA'88 and no regular proficiency testing is offered under CLIA.
- In the NYS program, cholinesterase was included in the June 2003 proficiency test event as an educational challenge.
- Equine serum cholinesterase added to chemistry proficiency testing samples.

1. **Identify the main components of the system.** The system consists of a **central processing unit (CPU)**, **memory**, **input devices**, and **output devices**.



# Lower Reference Limit Reported (U/L @ 37C)

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1800 Acetylcholine

1900\*

1900

1900

2100\*

2500

2900

3100

3167

3167

3200\*

3200

5400 Butyrylcholine

5600

5600

5900\*

5900\*

7000\*

8000\*

4000 Propionylcholine

\* Reported in U/mL (e.g. 1900 U/L = 1.9 U/mL)

# Cholinesterase Results for Two Serum Samples

	<u>Sample A</u> (U/L)	<u>Sample B</u> (U/L)
Acetylcholine (n=13)	2537 ± 346 (CV= 14%)	451 ± 104 (CV= 23%)
Butyrylcholine (n= 8)	6167 ± 1576 (CV= 26%)	1492 ± 551 (CV= 37%)
Propionylcholine	3528	977

# Cholinesterase Results

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- A total of 21 laboratories performed cholinesterase measurements; one laboratory reported results by two different methods.
- Cholinesterase testing is performed by only 1%\* of all of the laboratories in the NYS program: 14 outside NYS; 7 within NYS; and 2 outside the US.
- 13 laboratories used acetylcholine as a substrate and CV near the threshold activity (normal/toxic) was 13%
- 8 laboratories used butyrylcholine as a substrate and CV was 26%.

\* Two participants in this survey were not NYS certified laboratories;  $19/973 = 1.03\%$

# Summary & Conclusions

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- A relatively small number of laboratories nationwide offer testing services for cholinesterase.
- Agreement on lower normal threshold is poor.
- Interlaboratory agreement among the laboratories using the acetylcholine procedure is reasonably good.
- Proficiency testing is a convenient and useful manner to assess and evaluate laboratory infrastructure with a high degree of data quality.
- CDC National Laboratory Database expansion.



Thank you for your attention!

Bob Rej





# GREETINGS FROM NEW YORK



